A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds

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Version 1.0

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INVESTIGATOR ACKNOWLEDGMENT SIGNATURE

- I agree to conduct the study in accordance with the relevant, current protocol and will make changes in the protocol only after notifying the Sponsor, except when necessary to protect the safety, rights, or welfare of subjects.
- I agree to personally conduct and supervise the investigation as described within.
- I agree to inform all subjects that the device is being used for the purposes of an investigational study.
- I will ensure that requirements relating to obtaining informed consent in the guidelines for Good Clinical Practices, and 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.
- I agree to report to the Sponsor, IRB and/or Ethics Committee, according to the protocol, adverse experiences that occur during the course of the investigation in accordance with guidelines for Good Clinical Practices, and 21 CFR 812.
- I have read and understand the information in the protocol, including the potential risks.
- I agree to maintain adequate and accurate records in accordance with guidelines for Good Clinical Practices and 21 CFR 812.140 and to make those records available for inspection.
- I will ensure that an IRB compliant with the requirements of guidelines for Good Clinical Practices and 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others.
- I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in the guidelines for Good Clinical Practices, and the Code of Federal Regulations.

I have received and reviewed this Investigational Plan. I will conduct the study as described.

_____ _____

Investigator's Signature Date

DOCUMENT HISTORY

VERSION	DATE	DESCRIPTION
1.0	23-August-2018	Initial Release

1. PROTOCOL SUMMARY

1.1. Synopsis

Title:	A prospective case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds
Study Description:	Chronic wounds are a source of significant morbidity and escalating healthcare costs. The wound care professional has a myriad of modern wound dressings to choose from when treating a wound, each of which has benefits and drawbacks. An understanding of how a given dressing performs in healing a particular wound is crucial in order to determine a clinical mapping of wound dressings to wound types; such a categorization would lead to more efficient clinical decision making and better patient outcomes. This case series will evaluate the ability of a fibrillar collagen powder to improve healing of chronic, stalled, lower-extremity wounds.
Objectives:	Evaluate the ability of a fibrillar collagen powder dressing to treat chronic, stalled, lower-extremity wounds
Endpoints:	**Primary:** Change in wound size over twelve week period **Secondary:** 1) Change in Bates-Jensen Wound Assessment Tool score, 2) Change in reported pain level.
Study Population:	Twenty adult patients with chronic lower-extremity wounds (i.e. below the knee) of greater than four weeks that have failed to respond to at least one advanced wound dressing treatment. Specific wound types include: pressure ulcers, diabetic ulcers, and venous leg ulcers.
Phase:	Post-Market
Description of Sites/Facilities Enrolling Participants:	Outpatient podiatry clinics in the United States
Description of Study Intervention:	Patients who meet the inclusion criteria will be provided with fibrillar collagen powder dressing (Puracol® Ultra Powder by Medline Industries, Inc.). The powder dressing will be used in

accordance with its label. After cleansing the wound by the clinical site staff, the powder is placed directly on the wound, and then the wound will be covered with an appropriate moisture retentive secondary dressing. Patients will visit the clinic twice a week to have the powder re-applied. Wound evaluations will take place once a week at the outpatient clinic, with the intervention lasting up to twelve weeks. Concurrent standard of care, such as compression for venous ulcers, will be provided.

Study Duration: Total time for study completion to allow accrual of all subjects, and appropriate treatment as per the protocol, will be approximately 12-18 months

Participant Duration: Participant duration in the study will be a maximum of twelve weeks. In the event a participant's wound completely heals prior to the end of twelve weeks, his or her participation in the study will be complete at the time of complete wound healing.

1.2. Schedule of Activities (SOA)

REQUIRED ASSESSMENTS	PRE-SCREENING Day -1	SCREENING VISIT Day 0 (May be combined with Initial Visit, Day 1)	INITIAL VISIT Day 1	DRESSING CHANGE VISITS Twice weekly (Every 3 days ± 1 day)	WOUND ASSESSMENT VISITS Once per week Every 7 days ± 2 days (May be combined with Dressing Change Visit)	FINAL VISIT 12 weeks from Initial Visit[3]
Pre-Screening Questionnaire [1]	X					
Informed Consent		X				
Screening Form to assess eligibility		X				
Decision on eligibility		X				
Demographics			X			
Wound History			X			
Wound Photograph			X		X	X
Bates-Jensen Wound Assessment			X		X	X
Application of Puracol® Ultra			X	X	X[2]	
Pain Assessment for dressing change			X		X	X
Secondary Dressing Notation			X	X	X[2]	
Adverse Event Assessment		X	X	X	X	X
1: For participants contacting the research facility, 2: If combined with Dressing change visit, 3: Final visit may occur earlier in the event the participant's wound has completely healed before 12 weeks						

2. INTRODUCTION

2.1. Background & Rationale

Chronic wounds, defined as damage to epidermal or dermal structures present for greater than four weeks without significant clinical improvement, in spite of appropriate clinical management, represent a substantial burden on the healthcare system. Costs for venous leg ulcers, a wound type that often becomes chronic, were estimated at $3 billion annually as of 2006.[1] Other wound types, such as pressure ulcers and diabetic ulcers can also turn into chronic wounds, adding to healthcare costs and negatively impacting quality of life. These types of wounds frequently occur in the lower extremities due to venous or arterial insufficiency and pressure exerted on the foot or leg.

A key factor in wound healing is the production, deposition, and integration of collagen in the wound bed. Collagen is the most abundant protein in the human body, and it plays a key role in all phases of wound healing.[2] In chronic wounds, the deposition of *de novo* collagen is delayed and/or altered.[3,4] In these wounds there is both a reduction of collagen deposition, coupled with increased breakdown of the collagen that does get deposited, that prevents it from integrating into the wound bed and healing the wound.

In an effort to augment the formation and integration of collagen into the wound bed, healthcare professionals often turn to collagen based dressings. These dressings are composed of bovine, porcine, or avian collagen; the dressings are often in the form of a sheet that can be applied directly to the wound or a powder that is sprinkled over the wound. The influx of collagen aids in addressing the microenvironment of the wound, which may provide a different mechanism of action for healing compared to other advanced wound treatments, which often address the macro environment (e.g. moisture retentive dressings). Due to this, collagen dressings may be particularly useful for chronic wounds that have not responded to other advanced wound treatments, such as silver sulfadiazine, calcium alginate, or hydrocolloid dressings. Indeed, a case series of twenty patients with chronic, stalled wounds demonstrated the ability of a bovine-based collagen dressing to advance the healing of these wounds.[2] In the current study, a novel, porcine-based powder dressing will be evaluated in order to determine if it can achieve similar ends.

2.2. Investigational Product

Puracol® Ultra Powder collagen wound dressing is a powder-like fibrillar collagen microsponge composed of Type I porcine dermis collagen. The dressing is a currently marketed, cleared device in the United States, indicated for the management of full and partial thickness wounds, including: pressure ulcers, diabetic ulcers caused by mixed vascular origin, venous ulcers, and several other wound types. Appendix 11.1.1 provides the label and instructions for use (IFU) for the device.

As Puracol® Ultra comes in powder form, a secondary dressing applied over the wound is necessary. An appropriate sized dressing from the Optifoam® Gentle silicone border series by Medline Industries Inc., will be applied. Information pertaining to these dressings is provided in Appendix 11.1.2. Furthermore, given that the standard of care for patients with venous ulcers entails

application of a compression dressing, patients with these types of wounds will also receive CoFlex® TLC Two-Layer Compression System dressing; this dressing is currently marketed for the management of venous ulcers. More information regarding the CoFlex® TLC Two-Layer Compression System dressing is available in Appendix 11.1.3.

2.3. Risk/Benefit Profile

2.3.1. Potential Study Risks

Participants may experience irritation or a reddening due to the dressing. Participants will be under the care of a healthcare professional while using the dressing, and he or she will be able to intervene appropriately if the dressing causes any irritation or reddening.

2.3.2. Potential Study Benefits

Participants may experience a healing of their chronic, stalled wound as a result of the study product application.

2.3.3. Assessment of Potential Risk/Benefit Profile

The study product will be used in accordance with its currently marketed IFU, and the risks to participants are minor. Participants may experience healing of their wound through the application of the dressing. Due to this, the risk/benefit profile is favorable.

3. OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Evaluate the ability of a fibrillar collagen powder dressing to treat chronic, stalled, lower-extremity wounds.	**Primary** • Change in wound size	• A reduction in wound size is indicative of healing

	Secondary
	• Change in BWAT score
	• Change in reported pain level
	  o General pain level
	  o Pain level at dressing change
		• The BWAT is a validated tool for wound healing
		• Pain is indicative of healing and wound status

4. STUDY DESIGN

4.1. Overall Design

This is a prospective, open-label, case series investigating if a currently marketed collagen dressing can result in improved healing of chronic, stalled, lower-extremity wounds. An outpatient podiatry clinic will enroll twenty patients with qualifying wounds and monitor wound healing progress over the course of twelve weeks.

4.2. End of Study Definition

The conclusion of the study for an individual participant will occur at their last Wound Assessment Visit, which will be after twelve weeks of participation or when the wound is completely healed, whichever comes first. The study will be deemed complete upon issuance of the final Clinical Study Report.

5. STUDY POPULATION

5.1. Inclusion Criteria

In order to participate in the study, a participant must meet *ALL* of the following criteria:

- Age 18+
- Has one of the following types of wounds below the knee:
  - Diabetic ulcers
  - Pressure ulcers
  - Venous ulcers
  - Ulcers of mixed-vascular origin
  - Traumatic wounds
  - Post-surgical wounds
- Wound has been present for at least four weeks
- Wound is free of necrotic tissue or debridement practices will take place prior to initial visit in order to remove necrotic tissue.
- Wound has not responded to at least one type of advanced would care treatment
- Wound size is between 1 and 100 cm^2
- Patient has adequate circulation as demonstrated by biphasic or triphasic Doppler waveform, measured within three months prior to study enrollment. If monophasic on exam, then non-invasive tests must display Ankle Brachial Index greater than 0.8 and no worse than mild disease on segmental pressures.
- Wound is confirmed as being free of infection and absence of osteomyelitis.

5.2. Exclusion Criteria

A participant must not meet *ANY* of the criteria below to participate in the study

- Pregnant, planning to become pregnant during the study timeframe, or breast feeding
- Unable or unwilling to receive porcine collagen

- Wound is infected or presence of osteomyelitis
- Allergy or sensitivity to collagen
- Inability, in the opinion of the Investigator to follow protocol requirements, attend follow up visits in a timely manner, or otherwise comply with the requirements of the protocol

5.3. Strategies for Recruitment and Retention

The Principal Investigator (PI) maintains an outpatient podiatry clinic. The PI and/or site staff will offer enrollment to patients that may meet the inclusion/exclusion criteria. Participants will be provided with reminder notifications and documentation detailing their scheduled visits to the site.

6. STUDY PROCEDURES AND ASSESSMENTS

6.1. Day -1 – Pre-screening

Interested potential participants who contact the research site will undergo a brief pre-screening questionnaire via phone to determine initial eligibility. Potential participants will be assigned a screening number in order to de-identify the information on the form. The pre-screening form can be found in Appendix 11.2.1.

6.2. Day 0 - Informed Consent and Screening Visit

6.2.1. Informed Consent

Upon arrival to the study site, research staff will provide potential participants with a written informed consent form (ICF) that has received approval by an institutional review board (IRB) or Ethics Committee. The ICF will be written and administered in compliance with Good Clinical Practice (GCP) and comply with all elements required by FDA 21 CFR 50.25, International Conference on Harmonization (ICH), and state and local regulations. Research staff will answer any questions the potential participant has regarding the form. Written consent from the participant must be obtained prior to conducting any other research activities. A copy of the signed ICF will be offered to each participant.

6.2.2. Screening

After obtaining informed consent, research staff will assess eligibility to participate in the study using the screening form provided in Appendix 11.2.2. Participants who qualify will be assigned a subject number. In the event the potential subject has not had a measurement to determine adequate blood flow in the past three months, the PI or research staff will assess blood flow via a handheld vascular Doppler device. Subjects must meet the Doppler criteria mentioned in section 5.1 of this protocol to be randomized

6.3. Day 1 – Initial Visit

6.3.1. Demographic and Baseline Data Collection

The PI or research staff will collect the following demographic data and medical information: age, gender, race, height, weight, medical diagnoses, wound location, wound type, duration of wound, and prior treatments. These data will be recorded on the Initial Visit Case Report Form (CRF), provided in Appendix 11.3.1.

6.3.2. Photograph of Wound and Wound Size Measurement

Measurement of wound size will occur via software provided with an acceptable wound camera, to be provided by Medline. The PI will take a photograph of the wound with the camera and upload the file to a computer with appropriate software. The software will automatically calculate the wound size; this will serve as the wound size data point for the Initial Visit. Wound size, in cm^2 will be recorded on the Wound Photo CRF; a copy of the CRF is provided in Appendix 11.3.2.

6.3.3. Pain Assessment

Participants will verbally rate their perceived pain level twice during the visit. A "current" pain level will be captured by asking the participant his/her current pain during the visit; this measurement will be obtained at the beginning of the visit. If debridement is to be performed during the visit, the "current" pain evaluation will occur prior to debridement. Additionally, a pain level during dressing changes will also be acquired. Participants will use a 0-10 Verbal Numeric Pain Rating scale, with 0 corresponding to minimal pain and 10 indicating the worst pain imaginable. The value will be recorded on the Wound Photo CRF.

6.3.4. Bates-Jensen Wound Assessment Tool

The PI or research staff will administer the Bates-Jensen Wound Assessment Tool (BWAT) at the Initial Visit in order to gain an understanding of the wound characteristics. The instructions for use for the BWAT are provided in Section 11.3.3.1, with the actual tool that will serve as the CRF in Section 11.3.3.2. In order to convert the BWAT into a tool that is compatible with the idiosyncrasies of this study, a few minor changes were made. The field for "Name" was changed to "Subject Number." In addition, a field for "Date" and "Wound Assessment Number" were listed for tracking purposes, given the multiple visits that will occur with this study. Also, the BWAT contains three columns for scoring, each corresponding to a separate date and assessment. In this study there will likely be more than three visits for each subject, so we have deleted two of the columns to avoid confusion; a new BWAT CRF will be used for each visit. Similarly, the instructions to plot multiple scores on visual scale provided at the bottom of the assessment was removed; the score from that visit will be plotted elsewhere, and the trajectory of the scores will be analyzed after study completion using data from all visits.

6.3.5. Dressing Application

Following the wound assessment, the Investigator or other clinician on the research staff will cleanse the wound using a wound cleansing solution and apply the Puracol® Ultra Powder

dressing to the wound. A notation as to the type of secondary dressing applied will be noted on the Dressing Log CRF (see Appendix 11.3.4).

6.4. Dressing Change Visit

Participants will visit the clinic for a dressing change twice weekly. Ultimate determination of dressing change frequency will reside with the PI, in the event the twice weekly visits conflicts with the patient's clinical needs. During these visits, participants will be assessed for any Adverse Events (AEs) and have their dressing changed. Documentation of the dressing change will be captured in the Dressing Log CRF, available in Appendix 11.3.4.

6.5. Wound Assessment Visit

One of the dressing change visits will serve as the wound assessment visit as well. Participants will come to the clinic every 7 days ± 2 days so the PI can assess the wound. The assessments conducted at this visit will be identical to those described in Sections 6.3.2 to 6.3.4. Additionally, if the participant is due for a dressing change, one will occur at this visit as well. All events will be documented via the Wound Photograph, BWAT, and Dressing Log CRFs.

6.6. Final Visit

The Final Visit will take place 12 weeks after participant enrollment; in the event the wound completely heals before 12 weeks have passed, the visit where the PI notes complete wound healing will serve as the Final Visit. Data collection will follow the same procedures defined in Sections 6.3.1 to 6.3.4.

7. ADVERSE EVENTS

7.1. Definition of Adverse Event

The FDA definition for an AE will be used in this study: Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention related.

7.2. Definition of Serious Adverse Event

The FDA definition of a Serious Adverse Event (SAE) will be used in this study: An AE or suspected adverse reaction is considered "serious" if, in the view of either the PI or Sponsor, it results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions or,
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

7.3. Severity of Adverse Event

- **Mild:** Awareness of signs or symptoms, but easily tolerated; are of minor irritant type, causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs and symptoms are transient.
- **Moderate:** Discomfort severe enough to cause interference with usual activities; requiring treatment but not extended hospitalization or intensive care for the subject.
- **Severe:** Incapacitating with inability to do work or usual activities; signs and symptoms may be systemic in nature or require medical evaluation and/or treatment; requiring additional hospitalization or intensive care (prolonged hospitalization)

7.4. Relatedness of Adverse Event and Serious Adverse Event

- **Unrelated:** This category applies to those adverse events which, after careful consideration, are clearly and incontrovertibly due to extraneous causes (disease, environment, etc.)
- **Possible:** This category applies to those adverse events for which, after careful medical consideration at the time they are evaluated, a connection with the Investigational Product administration appears unlikely but cannot be ruled out with certainty.
- **Probable:** This category applies to those adverse events which, after careful medical consideration at the time they are evaluated, are felt with a high degree of certainty to be related to the Investigational Product.
- **Definite:** This category applies to those adverse events which, after careful consideration, are clearly and incontrovertibly due to the Investigational Product.

7.5. Expectedness

The PI will be responsible for determining whether an AE or SAE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

7.6. Adverse Event Reporting

AEs will be recorded on the Adverse Event form (Appendix 11.4) by the PI. Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity. Changes in severity will necessitate a new CRF to document the new level of severity. AEs characterized as intermittent require documentation of onset and duration of each episode.

Non-serious AEs are to be reported to the study Sponsor on a weekly basis for review, and reported to the IRB per IRB reporting requirements.

7.7. Serious Adverse Event Reporting

The study investigator shall complete an SAE Form (Appendix 11.5) and submit to the study Sponsor and to the reviewing IRB as soon as possible, but in no event later than 48 hours after the investigator first learns of the effect. The study Sponsor is responsible for conducting an evaluation of the SAE and shall report the results of such evaluation to the FDA and to all reviewing IRBs within 10 working days after the Sponsor first receives notice of the effect. Thereafter, the Sponsor shall submit such additional reports concerning the effect as FDA requests.

For questions regarding this process or the event, you may contact your Medline clinical designee or the Medline Associate Director of Clinical Operations:

Name: Kara Cassady
Phone: 847-643-3809
E-mail: kcassady@medline.com

8. STATISTICAL CONSIDERATIONS

8.1. Sample Size Determination

As this is an open-label, observational case series, meant to evaluate clinical use of the study product, a formal power analysis was not conducted. Rather, a sample of 20 participants was chosen to provide an initial estimate of product performance in a clinical setting. Data from this study may be used to perform a power analysis for larger, future trial.

8.2. Populations for Analyses

An evaluable dataset will be used to conduct all analyses. Participants who have at least a valid wound assessment at their Initial Visit and their Final Visit, and complied with at least 75% of the dressing changes, will be included in this dataset.

8.3. Data Analysis

8.3.1. Wound Size Analysis

Descriptive statistics for initial wound size (measured at the Initial Visit) and final wound size (measured at Final Visit) will be calculated. These statistics include measures of central tendency (e.g. mean, median), variability (e.g. standard deviation). A 95% confidence interval for mean wound size change will also be calculated, assuming normality of the data. For exploratory purposes, a paired samples t-test will be conducted on wound size at the Initial Visit vs. Final Visit to identify any significant differences in wound size over the course of the study; if the data are not normally distributed, a non-parametric test will be used. Finally, change in wound size over time, using data from each visit may be modeled, using other variables such as demographic and baseline data, to better understand predictors of wound closure.

8.3.2. BWAT Analysis

Descriptive statistics for BWAT score from the Initial Visit and the Final Visit will be calculated. Measures of central tendency and variability will also be provided, and a paired samples t-test conducted on the change in BWAT score from the Initial Visit and Final Visit will be calculated for exploratory purposes; non-parametric methods will be used if the data are not normally distributed. Further exploration of the data may occur via modeling BWAT score from each visit and including other variables such as demographic and baseline data to better understand predictors of wound closure.

8.3.3. Pain Scale Analysis

Descriptive measures of central tendency and variability will be provided for pain rating at the Initial Visit and the Final Visit. A 95% confidence interval for mean change in pain will also be calculated, assuming normality of the data. For exploratory purposes, paired samples t-test will be conducted on wound size at the Initial Visit vs. Final Visit to identify any significant differences in wound size over the course of the study; if the data are not normally distributed, a non-parametric test will be used. Though these data are technically on an ordinal scale, the ten-point scale allows for the mean value to be more informative, and for the potential of conducting parametric tests. Finally, change in pain over time may also be modeled similarly to change in wound size.

9. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

9.1. Key Roles and Study Governance

Principal Investigator
Emmy Oji, DPM
Valley Podiatry and Diabetic Foot Center
2550 Merced St. Fresno, CA 93721
559-256-9600

Name	Title	Affiliation	Responsibility
William Jacobson, PhD	Clinical Affairs Director	Medline Industries, Inc.	• Liaison with Investigators • Input on study design • Interpretation of results • General clinical and scientific oversight of study conduct
Jim Monti, PhD	Senior Medical Writer	Medline Industries, Inc.	• Authoring study protocol • Authoring final Clinical Study Report • Data analysis
Stephanie Martynenko	Clinical Research Associate I	Medline Industries, Inc.	• Study monitoring activities

9.2. Clinical Monitoring

The Clinical Research Associate (CRA) will confirm that the rights and well-being of subjects are protected, and that the reported trial data are accurate, complete, and verifiable from source documents. Moreover, the CRA will confirm the conduct of the trial by the PI and site is in compliance with the protocol, GCP, and regulatory requirements as well as any applicable institution or IRB and federal or local processes. Monitoring will occur at minimum every two months during the study duration or more frequently if:

- The volume or quality of data is large or there is a backlog of review due to unexpected issues
- This would also include any large volume of CRFs to be reviewed
- The site compliance with the protocol or compliance with expected ICH/GCP and regulatory requirements is lacking or there are continuing unresolved compliance issues
- There are unexpected AE/SAE or subject safety concerns noted
- There are any unexpected inconsistencies with study product management
- There is a request for more frequent monitoring by the site
- Any mutually agreeable situation as determined by the sites and Medline

The frequency of routine monitoring may be increased to a longer interval after three monitoring cycles if on-site situations support this change. CRA will discuss this with Medline Associate Director or Clinical Manager and will inform the PI prior to implementation.

Monitoring activities will include subject eligibility, source data review, CRF completion verification, product accountability, site continued suitability, PI study oversight, compliance, and all general monitoring activities as outlined in FDAs Code of Federal Regulations and ICH/GCP guidelines that guide that activity.

Medline Industries Inc. may, on occasion, contract with external CROs to provide CRA services and those CRAs are authorized to act on behalf of Medline Industries, Inc.

It is expected that the site will be compliant with any institutional SOPs during the execution of the protocol and evidence of that compliance should be readily documented and verifiable by the CRA.

The CRA will generate an internal Medline Industries Inc. visit report that will be filed with the Medline Industries, Inc. trial master file and will provide the PI a detailed follow-up letter after each monitoring visit that will outline the completed monitoring activities as well as any identified areas of concern and the expected/applicable corrections needed. Medline Industries Inc., reserves the right to perform audit of the study activities – either routine or for-cause – as needed, and may also perform clinical monitoring audit as well.

9.3. Regulatory and Ethical Considerations

9.3.1. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the PI, his or her staff, and the Sponsor. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Sponsor. All study data and study records will be managed and stored in accordance with the site's HIPAA compliant policies on data storage and security. All electronic transmission of data will adhere to HIPAA Security Rules.

The study monitor, other authorized representatives of the Sponsor, representatives of the IRB and regulatory agencies may inspect all documents and records required to be maintained by the PI, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

A master list linking subject numbers to patient name and medical record number will be maintained in a secure database by the PI. The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for at least a period of two years, or longer if dictated by the reviewing IRB, Institutional policies, Sponsor requirements, or ICH/GCP and FDA requirements. The PI will agree to notify Sponsor of any intent to move or destroy these documents.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be maintained at the research sites on the CRFs. Copies of the CRFs, which will not contain any identifiable information, will be provided to the Sponsor for the purposes of data analysis. The study data entry and study management systems used by clinical sites and by Medline Industries, Inc. research staff will be secured and stored in an access controlled locked drawer (any paper forms) and password protected (electronic records). At the end of the study, all study databases that are not already de-identified will be de-identified and archived at Medline Industries, Inc.

9.3.2. Safety Oversight

Given that this is a post-market study on a device used in accordance with its labeling, there is minimal safety risk to participants. The PI is a doctor of podiatric medicine and trained in treating these types of wounds. In the event there any AEs or SAEs, the PI will review them any make any necessary safety determinations as needed.

9.3.3. Data Handling and Record Keeping

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents of any kind (electronic, paper, etc.) should be completed in accordance with Good Documentation Practices (GDP) to ensure accurate interpretation of data. CRFs will be created for each subject. The CRA will verify the data entered into the CRF with the site source regardless of the type of source. The site will be responsible for developing a written process that ensures the CRA is able view the source data.

Data from the CRFs will be entered into an electronic spreadsheet via dual-entry to assure no errors. Data will be transferred to and analyzed with SAS for statistical analysis. SAS allows for internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Medline Industries, Inc. will be responsible for overseeing final data analysis and confirmation of results.

9.3.4. Study Records Retention

Study documents should be retained until at least two years have elapsed since the formal discontinuation of the study intervention or as required by any applicable FDA guidelines or for a longer period if required by local regulations. No records will be destroyed without the written consent of the Sponsor, if applicable. It is the responsibility of the Sponsor to inform the PI when these documents no longer need to be retained. The PI is required to notify Medline if the location of the stored documents is changed after it is defined at the time of the Close Out Visit at study end.

9.3.5. Study Discontinuation

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the PI, Sponsor, and IRB. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and Sponsor and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants as determined by AE review
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the Sponsor and/or IRB.

9.3.6. Study Closeout

Upon completion of the study, Medline and/or its designees will notify the site of closeout related procedures and will coordinate with the site the return of equipment and/or any unused

product. Medline CRA will communicate closely with the PI at that time point and will review all close out steps and materials. All study data, related study documents, and unused study product, will be returned to the Sponsor. Sponsor will provide the facility with a summary of the activities and findings after the final analysis of the data has been completed. The site will also notify the IRB that the study has completed.

9.3.7. Conflict of Interest Policy

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication or any aspect of this trial will be disclosed and managed.

9.4. Protocol Deviations

It is the responsibility of the PI and study staff to use continuous vigilance to identify and report deviations on a routine basis. All deviations must be addressed in study source documents, and reported to Medline Industries, Inc. Protocol deviations must be sent to the reviewing IRB per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements

9.5. Abbreviations and Terms

AE	Adverse Event
BWAT	Bates-Jensen Wound Assessment Tool
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
CRF	Case Report Form
DPM	Doctor of Podiatric Medicine
GCP	Good Clinical Practice
GDP	Good Documentation Practice
ICH	International Conference on Harmonization
IFU	Instructions for Use
IRB	Institutional Review Board
PI	Principal Investigator

10. REFERENCES

1. Bergan JJ, Schmid-Schonbein GW, Coleridge Smith PD, Nicolaides AN, Boisseau MR, Eklof B. Mechanisms of disease: chronic venous disease. *N Engl J Med*. 2006;355:488-98.
2. Shah SV, Chakravarthy, D. Evaluation of a bovine 100% native collagen for the treatment of chronic wounds: A case series. *J Wound Ostomy Continence Nurs*. 2015 May-Jun;42(3):226-34.
3. Herrick SE, Ireland GW, Simon D, McCollum CN, Ferguson MW. Venous ulcer fibroblasts compared with normal fibroblasts show differences in collagen but not fibronectin production under both normal and hypoxic conditions. *J Invest Dermatol.* 1996;106:187-93.
4. Falanga V. Chronic wounds: pathophysiologic and experimental considerations. *J Invest Dermatol.* 1993;100:721-25.

11. APPENDIX

11.1. Products used in study

11.1.1. Investigational Product: Puracol® Ultra Powder Label and Instructions for Use

1-800-MEDLINE
www.medline.com

Instructions For Use

PURACOL® ULTRA
POWDER COLLAGEN
WOUND DRESSING

1-800-MEDLINE
www.medline.com

Description

PURACOL® ULTRA POWDER is a powder-like fibrillar collagen microsponge, a native primarily Type I porcine dermis collagen that is composed of specific amino acids. The building blocks that make up collagen are called amino acids. Collagen is primarily present in connective tissue and found in skin, tendon and ligament. **PURACOL® ULTRA** POWDER is a sterile wound exudate absorber and filler. **PURACOL® ULTRA** POWDER protects the wound bed and delicate newly regenerated granulation tissue. **PURACOL® ULTRA** POWDER interacts with the wound by absorbing the wound's fluids forming a gel-like barrier and provides a moist healing environment.

INDICATIONS FOR USE:
PURACOL® ULTRA POWDER is indicated for the management of full and partial thickness wounds including; pressure ulcers, diabetic ulcers caused by mixed vascular origin, venous ulcers, donor and graft sites, abrasions, traumatic wounds healing by secondary intention, dehisced surgical wounds, first and second degree burns.

WARNINGS AND PRECAUTIONS:
- For external use only.
- If redness, swelling or bleeding continues, seek the help of a medical professional.
- Do not use on individuals with a known sensitivity to collagen.
- Product is provided sterile in unopened, undamaged packaging. Do not use if the package has been opened prior to receipt or damaged in anyway.
- **PURACOL® ULTRA** POWDER collagen wound dressing is for single patient use, single use only. Unused product must be discarded.
- Caution: Federal (USA) Law restricts this device to sale by or on the order of a physician or properly licensed health care professional.

INSTRUCTIONS FOR USE:
1. Cleanse the burn or wound in accordance with normal procedures.
2. Apply, from the product envelope, a uniform layer of **PURACOL® ULTRA** POWDER directly into the wound site.
3. Cover the wound with an appropriate moisture retentive secondary dressing.
   NOTE: Superficial wounds such as cuts and abrasions may not require a secondary dressing due to the film that forms on the wound site if permitted to dry.
4. Reapply **PURACOL® ULTRA** POWDER and redress as needed.

REMOVAL INSTRUCTIONS:
PURACOL® ULTRA POWDER does not need to be removed from the wound site. Puracol® Ultra Powder is naturally broken down in the wound healing process.

CHANGE FREQUENCY:
As needed or as indicated by the amount of drainage.

STORAGE:
Store in dry conditions at room temperature (59-86°F). Extreme temperatures may denature collagen, but will not affect performance of product.

Single use only.
Sterility guaranteed in unopened, undamaged package.
This product is not made with Natural Rubber Latex.

REF

MSC8801EP

Size:
PURACOL® ULTRA POWDER, 1 gram envelope

Estimated Dressing Yield*:
(for 4x4", 10cmx10cm surface area)
2"x2" surface area

DEFINITION OF SYMBOLS:

LOT - Lot number

- Expiration date

1-800-MEDLINE
www.medline.com

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Medline Industries, Inc., Northfield, IL 60093 USA.

RC17VBL

11.1.2. Optifoam® Gentle Silicone Border Dressings

Optifoam Gentle silicone border dressings are currently marketed dressings indicated for the management of partial and shallow full-thickness wounds. The dressings aid in providing a moist wound environment and the absorption of exudate, which aids in wound healing. The silicone adhesive is often less traumatic and painful upon removal compared to acrylic based adhesives. The dressings that will be used in this study are available in four sizes: 1/6" × 2", 3" × 3", 4" × 4", and 6" × 6".

11.1.3. CoFlex® TLC Two Layer Compression Bandage System

CoFlex TLC two-layer compression bandage system is a compressive dressing system intended for use to manage venous disease. The first layer of the dressing is a soft foam that wicks away moisture, with the second layer composed of a short stretch cohesive material, providing adaptive compression levels. The device also comes with a nylon stocking to apply over the completed dressing for patient comfort and ease of movement under clothes and on bed sheets. Further information regarding the device can be found below or at https://www.medline.com/product/CoFlex-TLC-Two-Layer-Compression-System/Multi-Layer-Compression-Systems/Z05-PF11482?question=coflex+tlc&index=P1&indexCount=1

11.2. Screening Forms

11.2.1. Pre-Screening Form

Pre-Screening Form MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds	
Screening #:	**Criteria**
Age: _____	Between ≥ 18
Where is your wound located? _____	Must be below knee
How long has the wound been present? _____	Must be ≥ 4 weeks
Have you tried any therapies to heal the wound? If so, what were they? _____	Must have tried at least one type of advanced wound dressing/therapy
Would you be able to visit the clinic twice a week for up to 12 weeks? _____	Must answer yes

This subject is: Continuing in the study ☐ Dismissed from the study ☐

If subject is dismissed, please document reason: _____

Form completed by: _____ Date: _____

11.2.2. Screening Form

Screening Form

MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds

Subject #: __ __ __ __ __	Age: _____	
Gender (please check on): ☐ Male ☐ Female	**Yes**	**No**
Exclusion Criteria		
1. Does the subject have a known sensitivity to collagen?	☐	☐
2. Is the subject pregnant, breast feeding, or intending to become pregnant during the duration of the study?	☐	☐
3. Does patient have osteomyelitis or an infection in the wound?	☐	☐
4. Is the subject unwilling or unable to apply a porcine based product to the wound?	☐	☐
Inclusion Criteria		
5. Is the wound located below the knee?	☐	☐
6. Is the chronic wound between 1 cm^2 to 100 cm^2	☐	☐
7. Is the subject's wound duration greater than or equal to four weeks?	☐	☐
8. Is the wound a pressure ulcer, diabetic foot ulcer, venous ulcer, ulcer of mixed-vascular origin, post-surgical, or traumatic wound (circle wound type)	☐	☐
9. Has the subject tried an advanced wound dressing or therapy to treat the wound without success? If yes, list below:_____	☐	☐
10. Biphasic or triphasic Doppler waveform, or Ankle Brachial Index > 0.8 with no worse than mild disease on segmental pressures, taken within last 3 months	☐	☐

To qualify for study, subject must:

- be ≥ 18 years old
- Have a "No" response for questions 1-4
- Have a "Yes" response for questions 5-9

This subject is: Continuing in the study ☐ Dismissed from the study ☐

If subject is dismissed, please document reason: _____

Form completed by: _____ Date: _____

11.3. Case Report Forms

11.3.1. Initial Visit Case Report Form

Initial Visit Case Report Form

MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds

Demographic Data

Subject Number:	**Age:**	**Gender:** Male ❒ Female ❒
Height (in):	**Weight (lbs):**	

Race (may select more than one): Black ☐ White ☐ Asian ☐ Hispanic ☐ Other ☐

Relevant Medical Diagnoses and Current Medications:

Wound History

Wound Type:

Wound Location:

Duration of wound (in months):

Prior treatments and duration:	
Has mechanical debridement been performed?	**Yes** ☐ **No** ☐

Form Completed by:	**Date:**

11.3.2. Wound Photo Case Report Form

Wound Photo Case Report Form

MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds

Place photograph of the wound below:

Subject Number: _____ **Date:** _____ **Wound Assessment Number:** _____

Wound Size: _____ cm^2 (enter value obtained from camera software platform)

Current Pain Rating: _____ **Dressing Change Pain Rating:** _____

11.3.3. Bates-Jensen Wound Assessment Tool (BWAT)

11.3.3.1. BWAT Instructions for use

General Guidelines:

Fill out the attached rating sheet to assess a wound's status after reading the definitions and methods of assessment described below. Evaluate once a week and whenever a change occurs in the wound. Rate according to each item by picking the response that best describes the wound and entering that score in the item score column for the appropriate date. When you have rated the wound on all items, determine the total score by adding together the 13-item scores. The HIGHER the total score, the more severe the wound status. Plot total score on the Wound Status Continuum to determine progress. If the wound has healed/resolved, score items 1,2,3 and 4 as =0.

Specific Instructions:

1. **Size**: Use ruler to measure the longest and widest aspect of the wound surface in centimeters; multiply length x width. Score as = 0 if wound healed/resolved.

2. **Depth**: Pick the depth, thickness, most appropriate to the wound using these additional descriptions, score as
   0 = if wound healed/resolved:
   1 = tissues damaged but no break in skin surface.
   2 = superficial, abrasion, blister or shallow crater. Even with, &/or elevated above skin surface (e.g., hyperplasia).
   3 = deep crater with or without undermining of adjacent tissue. 4 = visualization of tissue layers not possible due to necrosis. 5 = supporting structures include tendon, joint capsule.

3. **Edges**: Score as = 0 if wound healed/resolved. Use this guide:

Indistinct, diffuse	=	unable to clearly distinguish wound outline.
Attached	=	even or flush with wound base, no sides or walls present; flat.
Not attached	=	sides or walls are present; floor or base of wound is deeper than edge.
Rolled under, thickened	=	soft to firm and flexible to touch.
Hyperkeratosis	=	callous-like tissue formation around wound & at edges.
Fibrotic, scarred	=	hard, rigid to touch.

4. **Undermining**: Score as = 0 if wound healed/resolved. Assess by inserting a cotton tipped applicator under the wound edge; advance it as far as it will go without using undue force; raise the tip of the applicator so it may be seen or felt on the surface of the skin; mark the surface with a pen; measure the distance from the mark on the skin to the edge of the wound. Continue process around the wound. Then use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.

5. **Necrotic Tissue Type**: Pick the type of necrotic tissue that is predominant in the wound according to color, consistency and adherence using this guide:

White/gray non-viable tissue	=	may appear prior to wound opening; skin surface is white or gray.
Non-adherent, yellow slough	=	thin, mucinous substance; scattered throughout wound bed; easily separated from wound tissue.
Loosely adherent, yellow slough	=	thick, stringy, clumps of debris; attached to wound tissue.
Adherent, soft, black eschar	=	soggy tissue; strongly attached to tissue in center or base of wound.
Firmly adherent, hard/black eschar	=	firm, crusty tissue; strongly attached to wound base and edges (like a hard scab).

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6. **Necrotic Tissue Amount**: Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.

7. **Exudate Type**: Some dressings interact with wound drainage to produce a gel or trap liquid. Before assessing exudate type, gently cleanse wound with normal saline or water. Pick the exudate type that is predominant in the wound according to color and consistency, using this guide:

Bloody	=	thin, bright red
Serosanguineous	=	thin, watery pale red to pink
Serous	=	thin, watery, clear
Purulent	=	thin or thick, opaque tan to yellow or green may have offensive odor

8. **Exudate Amount**: Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie- shaped quadrants to determine percent of dressing involved with exudate. Use this guide:

None	=	wound tissues dry.
Scant	=	wound tissues moist; no measurable exudate.
Small	=	wound tissues wet; moisture evenly distributed in wound; drainage involves ≤25% dressing.
Moderate	=	wound tissues saturated; drainage may or may not be evenly distributed in wound; drainage involves > 25% to ≤75% dressing.
Large	=	wound tissues bathed in fluid; drainage freely expressed; may or may not be evenly distributed in wound; drainage involves > 75% of dressing.

9. **Skin Color Surrounding Wound**: Assess tissues within 4cm of wound edge. Dark-skinned persons show the colors "bright red" and "dark red" as a deepening of normal ethnic skin color or a purple hue. As healing occurs in dark-skinned persons, the new skin is pink and may never darken.

10. **Peripheral Tissue Edema & Induration**: Assess tissues within 4cm of wound edge. Non-pitting edema appears as skin that is shiny and taut. Identify pitting edema by firmly pressing a finger down into the tissues and waiting for 5 seconds, on release of pressure, tissues fail to resume previous position and an indentation appears. Induration is abnormal firmness of tissues with margins. Assess by gently pinching the tissues. Induration results in an inability to pinch the tissues. Use a transparent metric measuring guide to determine how far edema or induration extends beyond wound.

11. **Granulation Tissue**: Granulation tissue is the growth of small blood vessels and connective tissue to fill in full thickness wounds. Tissue is healthy when bright, beefy red, shiny and granular with a velvety appearance. Poor vascular supply appears as pale pink or blanched to dull, dusky red color.

12. **Epithelialization**: Epithelialization is the process of epidermal resurfacing and appears as pink or red skin. In partial thickness wounds it can occur throughout the wound bed as well as from the wound edges. In full thickness wounds it occurs from the edges only. Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved and to measure the distance the epithelial tissue extends into the wound.

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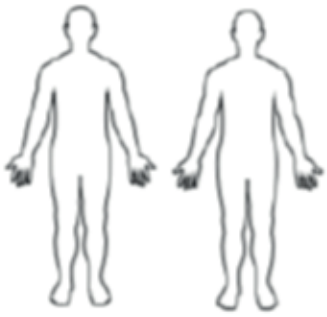
11.3.3.2. BWAT Case Report Form

Subject Number: _____ Date:_____ Assessment Number: _____

Complete the rating sheet to assess wound status. Evaluate each item by picking the response that best describes the wound and entering the score in the item score column for the appropriate date. If the wound has healed/resolved, score items 1,2,3, & 4 as =0.
Location: Anatomic site. Circle, identify right (R) or left (L) and use "X" to mark site on body diagrams:

Sacrum & coccyx	Lateral ankle
Trochanter	Medial ankle
Ischial tuberosity	Heel
Buttock	Other site:



Shape: Overall wound pattern; assess by observing perimeter and depth.

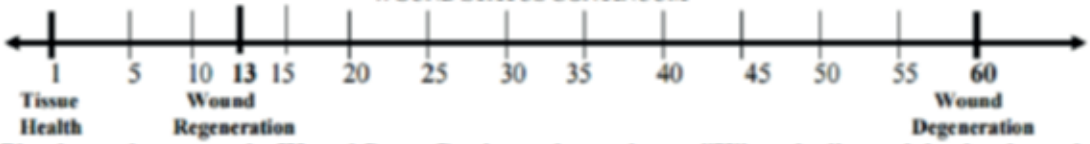
Circle and date appropriate description:

Irregular	Linear or elongated	
Round/oval	Bowl/boat	
Square/rectangle	Butterfly	Other Shape

Item	Assessment	Date Score
1. Size*	*0 = Healed, resolved wound 1 = Length x width <4 sq cm 2 = Length x width 4--≤16 sq cm 3 = Length x width 16.1--≤36 sq cm 4 = Length x width 36.1--≤80 sq cm 5 = Length x width >80 sq cm	
2. Depth*	*0 = Healed, resolved wound 1 = Non-blanchable erythema on intact skin 2 = Partial thickness skin loss involving epidermis &/or dermis 3 = Full thickness skin loss involving damage or necrosis of subcutaneous tissue; may extend down to but not through underlying fascia; &/or mixed partial & full thickness &/or tissue layers obscured by granulation tissue 4 = Obscured by necrosis 5 = Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures	
3. Edges*	*0 = Healed, resolved wound 1 = Indistinct, diffuse, none clearly visible 2 = Distinct, outline clearly visible, attached, even with wound base 3 = Well-defined, not attached to wound base 4 = Well-defined, not attached to base, rolled under, thickened 5 = Well-defined, fibrotic, scarred or hyperkeratotic	
4. Under- mining*	*0 = Healed, resolved wound 1 = None present 2 =Undermining < 2 cm in any area 3 = Undermining 2-4 cm involving < 50% wound margins 4 = Undermining 2-4 cm involving > 50% wound margins 5 = Undermining > 4 cm or Tunneling in any area	
5. Necrotic Tissue Type	1 = None visible 2 = White/grey non-viable tissue &/or non-adherent yellow slough 3 = Loosely adherent yellow slough 4 = Adherent, soft, black eschar 5 = Firmly adherent, hard, black eschar	

6. Necrotic Tissue Amount	1 = None visible 2 = < 25% of wound bed covered 3 = 25% to 50% of wound covered 4 = > 50% and < 75% of wound covered 5 = 75% to 100% of wound covered	
7. Exudate Type	1 = None 2 = Bloody 3 = Serosanguineous: thin, water, pale red/pink 4 = Serous: think, watery, clear 5 = Purulent: thin or thick, opaque, tan/yellow, with or without odor	
8. Exudate Amount	1 = None, dry wound 2 = Scant, wound moist but no observable exudate 3 = Small 4 = Moderate 5 = Large	
9. Skin Color Surrounding Wound	1= Pink or normal for ethnic group 2 = Bright red &/or blanches to touch 3 = White or grey pallor or hypopigmented 4 = Dark red or purple &/or non-blanchable 5 = Black or hyperpigmented	
10. Peripheral Tissue Edema	1 = No swelling or edema 2 = Non-pitting edema extends < 4cm around wound 3 = Non-pitting edema extends ≥ 4cm around wound 4 = Pitting edema extends < 4cm around wound 5 = Pitting edema extends ≥ 4cm around wound	
11. Peripheral Tissue Induration	1 = None present 2 = Induration < 2cm around wound 3 = Induration 2-4cm extending <50% around wound 4 = Induration 2-4cm extending ≥50% around wound 5 = Induration > 4cm in any area around wound	
12. Granulation Tissue	1 = Skin intact or partial thickness wound 2 = Bright, beefy red; 75% to 100% of wound filled &/or tissue overgrowth 3 = Bright, beefy red; <75% & >25% of wound filled 4 = Pink, &/or dull, dusky red &/or fills ≤25% of wound 5 = No granulation tissue present	
13. Epithelialization	1 = 100% wound covered, surface intact 2 = 75% to < 100% wound covered &/or epithelial tissue extends > 0.5cm into wound bed 3= 50% to < 75% wound covered &/or epithelial tissue extends < 0.5cm into wound bed 4 = 25% to < 50% wound covered 5 = < 25% wound covered	
Total Score		
Signature		

WOUND STATUS CONTINUUM



Plot the total score on the Wound Status Continuum by putting an "X" on the line and the date beneath the line.

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11.3.4. Dressing Log Case Report Form

Dressing Log Case Report Form MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds	
Subject Number:	
Change #1 Date:	**Secondary Dressing(s) Applied:**
Change #2 Date:	**Secondary Dressing(s) Applied:**
Change #3 Date:	**Secondary Dressing(s) Applied:**
Change #4 Date:	**Secondary Dressing(s) Applied:**
Change #5 Date:	**Secondary Dressing(s) Applied:**
Change #6 Date:	**Secondary Dressing(s) Applied:**
Change #7 Date:	**Secondary Dressing(s) Applied:**
Change #8 Date:	**Secondary Dressing(s) Applied:**
Change #9 Date:	**Secondary Dressing(s) Applied:**
Change #10 Date:	**Secondary Dressing(s) Applied:**
Change #11 Date:	**Secondary Dressing(s) Applied:**
Change #12 Date:	**Secondary Dressing(s) Applied:**
Change #13 Date:	**Secondary Dressing(s) Applied:**
Change #14 Date:	**Secondary Dressing(s) Applied:**
Change #15 Date:	**Secondary Dressing(s) Applied:**

Dressing Log Case Report Form MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds	
Change #15 Date:	**Secondary Dressing(s) Applied:**
Change #16 Date:	**Secondary Dressing(s) Applied:**
Change #17 Date:	**Secondary Dressing(s) Applied:**
Change #18 Date:	**Secondary Dressing(s) Applied:**
Change #19 Date:	**Secondary Dressing(s) Applied:**
Change #20 Date:	**Secondary Dressing(s) Applied:**
Change #21 Date:	**Secondary Dressing(s) Applied:**
Change #22 Date:	**Secondary Dressing(s) Applied:**
Change #23 Date:	**Secondary Dressing(s) Applied:**
Change #24 Date:	**Secondary Dressing(s) Applied:**
Change #25 Date:	**Secondary Dressing(s) Applied:**
Change #26 Date:	**Secondary Dressing(s) Applied:**
Change #27 Date:	**Secondary Dressing(s) Applied:**
Change #28 Date:	**Secondary Dressing(s) Applied:**
Change #29 Date:	**Secondary Dressing(s) Applied:**
Change #30 Date:	**Secondary Dressing(s) Applied:**
Change #31 Date:	**Secondary Dressing(s) Applied:**

Dressing Log Case Report Form MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds	
Change #32 Date:	**Secondary Dressing(s) Applied:**
Change #33 Date:	**Secondary Dressing(s) Applied:**
Change #33 Date:	**Secondary Dressing(s) Applied:**
Change #34 Date:	**Secondary Dressing(s) Applied:**
Change #35 Date:	**Secondary Dressing(s) Applied:**
Change #36 Date:	**Secondary Dressing(s) Applied:**
Change #37 Date:	**Secondary Dressing(s) Applied:**
Change #38 Date:	**Secondary Dressing(s) Applied:**
Change #39 Date:	**Secondary Dressing(s) Applied:**
Change #40 Date:	**Secondary Dressing(s) Applied:**
Change #41 Date:	**Secondary Dressing(s) Applied:**
Change #42 Date:	**Secondary Dressing(s) Applied:**
Change #43 Date:	**Secondary Dressing(s) Applied:**
Change #44 Date:	**Secondary Dressing(s) Applied:**
Change #45 Date:	**Secondary Dressing(s) Applied:**
Change #46 Date:	**Secondary Dressing(s) Applied:**
Change #47 Date:	**Secondary Dressing(s) Applied:**

Dressing Log Case Report Form MED-2018-DIV71-008: A case series evaluating a fibrillar collagen powder dressing to treat chronic, stalled lower-extremity wounds	
Change #48 Date:	**Secondary Dressing(s) Applied:**
Change #49 Date:	**Secondary Dressing(s) Applied:**
Change #50 Date:	**Secondary Dressing(s) Applied:**
Change #51 Date:	**Secondary Dressing(s) Applied:**
Change #52 Date:	**Secondary Dressing(s) Applied:**
Change #53 Date:	**Secondary Dressing(s) Applied:**
Change #54 Date:	**Secondary Dressing(s) Applied:**
Change #55 Date:	**Secondary Dressing(s) Applied:**
Change #56 Date:	**Secondary Dressing(s) Applied:**
Change #57 Date:	**Secondary Dressing(s) Applied:**
Change #58 Date:	**Secondary Dressing(s) Applied:**
Change #59 Date:	**Secondary Dressing(s) Applied:**
Change #60 Date:	**Secondary Dressing(s) Applied:**
Change #61 Date:	**Secondary Dressing(s) Applied:**
Change #62 Date:	**Secondary Dressing(s) Applied:**
Change #63 Date:	**Secondary Dressing(s) Applied:**

11.4. Adverse Event Form

Site/Subject Information	
Study Sponsor: Medline Industries, Inc.	Protocol Number: MED-2018-DIV71-008
Site Number:	Principal Investigator:
Subject Number:	

Adverse Event Information

#	Adverse Event:		Start Date: DD-MMM-YYYY	Stop Date: DD-MMM-YYYY	Ongoing:	Frequency:	Severity:	Outcome:	IP Lot #:	Relation-ship to IP:	Action Taken with IP:	SAE Status:	Comment:
		☐ Expected			☐ Yes							☐ Yes*	
		☐ Unexpected			☐ No							☐ No	
		☐ Expected			☐ Yes							☐ Yes*	
		☐ Unexpected			☐ No							☐ No	
		☐ Expected			☐ Yes							☐ Yes*	
		☐ Unexpected			☐ No							☐ No	

Frequency:	Severity:	Outcome:	Relationship to IP:	Action Taken with IP:	SAE Status
1 = Isolated 2 = Intermittent 3 = Continuous	1 = Mild 2 = Moderate 3 = Severe	1 = Resolved, with no sequelae 2 = Resolved, with sequelae 3 = Unresolved 4 = Death 5 = Unknown	1 = Not Related 2 = Possible 3 = Probable 4 = Definite	1 = None 2 = Modified 3 = Interrupted 4 = Discontinued	Death, life-threatening, prolonged hospitalization, significant disability/anomaly, medical intervention to prevent a serious outcome

***In the event of a Serious Adverse Event, please complete the Serious Adverse Event Report form and send to Medline Industries, Inc. within 48 hours of awareness**

11.5. Serious Adverse Event

Site Information		
Study Sponsor: Medline Industries Inc.	Protocol Number: MED-2018-DIV71-008	
Site Number:	Principal Investigator:	
Site Address:	Report Type:	☐ Initial
		☐ Follow-up
		☐ Final
Form Completed By:	Title:	
Telephone:	E-mail:	

Serious Adverse Event Information			
Subject Number:	Subject Initials:		
Birth Date:	Gender:	☐ Male	☐ Female
Investigational Product:			
Event Description: (Please include a detailed description of the event in question, including the results of any laboratory/diagnostic imagery testing)			
Site Notification of the Event:	Date Notified:	Time Notified:	
	Method of Notification:		
Event Start/Stop:	Start Date:	Stop Date:	☐ Ongoing
Event Qualifiers: (Check all that apply)	☐ Death	☐ Intervention to Prevent Impairment	
	☐ Life-Threatening	☐ Disability/Permanent Damage	
	☐ Initial or Prolonged Hospitalization	☐ Congenital Anomaly	
	☐ Other:		

Relevant Medical History:	
Concomitant Medication/Device History: (Please include historical information such as medication/device name, dosage, frequency, route, start date, etc.)	
Relationship to Investigational Product (IP):	☐ Not Related (event definitely not related to IP, as judged by the Principal Investigator)
	☐ Possibly Related (event maybe related to IP, as judged by the Principal Investigator)
	☐ Related (event definitely related to IP, as judged by the Principal Investigator)
Action Taken with Investigational Product:	☐ Discontinued- Please Provide Date:
	☐ Interrupted- Please Provide Date:
	☐ None
Comments:	

Confirmation of Receipt: SECTION TO BE COMPLETED BY MEDLINE INDUSTRIES INC.	
Date Received:	Time Received:
Received By:	Title: